Author's response to reviews

Title: Behavioral and Technological Interventions Targeting Glycemic Control in a Racially/Ethnically Diverse Population: A Randomized Controlled Trial

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Author's response to reviews: see over
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Dear Editor:

We thank you and the three kind reviewers for the opportunity to revise our manuscript for publication consideration in the BMC Public Health. We have revised our manuscript in light of the reviewers’ comments and made all the required changes to the format of the paper. We addressed the comments as follows:

REVIEWER 1 (GURPRATAAP SANDHU)

MAJOR COMPULSORY REVISIONS:
Comment
Abstract: My understanding is that there are 2 main goals of this study. To compare the effectiveness of 2 different diabetes self care interventions on glycemic control AND whether HgbA1c reduction was ‘more marked’ in minority patients. Abstract needs to clearly mention the results for your aims (the aim that whether minorities will have ‘more’ reduction in A1c is not mentioned in the abstract). It only says that there is modest reduction in all racial groups.
Response
A sentence has been inserted in the revised Abstract to clearly mention that there was no marked reduction in minority patients.

Comment
P value for the main results needs to mentioned in the abstract.
Response
P-value for the main result (P=.771) has been included in the revised abstract.

Comment
Is the conclusion justified based on the results? There was no statistically significant change from baseline in HgbA1c
Response
We believe the conclusion is justified since there were indeed modest reductions in all study arms, albeit there was no statistically change from baseline.

Comment
Since this a RCT and you don’t expect any statistically significant difference at baseline in A1C, can the authors please perform a simple ANOVA on the A1c values at 12 months and see if there is a difference that is statistically significant.
Response
We did perform an ANOVA test as described in the Statistical Analysis section (p.9) and reported in the Results section (p.12), which indicated that HbA1c values at 12 months were not statistically different (P =.771).

MINOR ESSENTIAL REVISIONS:
Comment
Table 2:
Would highly recommend to restructure the table in simple terms (using language and major p values if necessary), as the clinical audience of the journal might not be well versed with advanced statistics. SE and 95% CI in the same table is redundant. Also consider excluding z value in the table, as it does not add not much information. What was the reason that authors used reductions in HgbA1c ‘per day’ over the 12 months period. For the clinical audience, this might not be useful information, as there is no need to repeat A1c for at least 3 months.

Response
A multilevel, longitudinal model was utilized to determine whether treatments had an effect on the rate of change in the level of HbA1c over time. Time was set as a continuous variable in days, since HbA1c values had dates of assessment. We were able to calculate how many days from baseline each HbA1c value was measured based on these dates. Because of this, we included time as a continuous variable, measured in days, from baseline (defined as 0). We realize that changes per day may not be relevant for the clinical audience and thus have also provided changes in HbA1c from baseline to 12-months of follow-up in the Abstract and the Results section.

We believe that this is the best way to present our results based on the model we chose. In fact, it was to the benefit of the clinical audience that we decided to report SEs, CIs, and z-values, although we agree that they may be somewhat redundant.

Comment
Statistical analysis- Para 3, in sample size estimation, what is considered a statistically significant changes in A1c. By that I mean what % change (for 80% power and two sided significance of 0.05).

Response
The power analysis was constructed to see a 0.5% change in HbA1c. This was inadvertently left out and has now been inserted in the revised paper.

DISCRETIONARY REVISIONS:
Comment
Consider publishing Table 3 as a supplementary table.

Response
Again we believe that this is the best way to present the results based on the model we chose.

Comment
Data collection- Paragraph 3 and 4 can be shortened

Response
We have shortened paragraphs 3 and 4 substantially as recommended.

Comment
Results: Participant Adherence/Engagement with Interventions could be merged with Results: paragraph 1.
Response
The section on participant adherence has been moved under the first section of the Results, (p. 10), which has now been changed to “Subject Enrollment, Participation, Retention, and Adherence.”

Comment
Discussion Paragraph 1 last line seems to be disjointed with paragraph 2 1st line. Please consider editing.
Response
We have reconciled the two paragraphs by deleting the last sentence of paragraph 1.

Comment
Discussion para 6 line 1: please consider changing the word 'somewhat consistent', as it does not provide much information to the reader
Response
We have deleted “somewhat” from the sentence.

Comment
Please consider editing Para 6 of discussion. It is not clear what you are trying to compare; the baseline A1c among racial groups or change in A1c after intervention. Would recommend to stay consistent.
Response
We have revised paragraph accordingly by deleting the last two sentences.

Comment
Based on your results, do the authors feel that PDAs are a viable strategy in the future (given the fact, as the authors themselves mentioned, a much higher attrition rate in the 2 groups that used PDAs; costs associated with buying an additional device and training personnel; and with the smart phone era upon us). I think the discussion section will benefit from a recommendation in this regard.
Response
We have included the following to the Discussion section in the first paragraph on p.15, “However, it may be more beneficial to shift our focus from diabetes self-management software designed for PDAs to more mainstream devices such as smartphones and tablets. These devices have already been accepted by the general public and integrating diabetes self-management programs on these platforms would yield a more seamless transition into an individual’s daily routine.”

Comment
I wonder why you chose an A1c of >7.5% or greater as your inclusion criteria, when the current guidelines suggest a goal A1C of <7%. Maybe a difference could have been observed if a higher A1c inclusion criteria (e.g. 8% as in your pilot study) was used. Is it possible for you to do a subgroup analysis based on A1c sub-categories (with the understanding that the results might be insignificant because of just being underpowered).
Response
HbA1c values ≤7% are common treatment targets for individuals with T2DM. For the purposes of our study, we wanted to look at reductions in HbA1c levels among individuals with uncontrolled diabetes. As such, we focused on individuals with baseline levels of HbA1c greater than 7.5%. Initially, we had 8.0% as our cut point for study inclusion, but reduced this to allow for the margin of error in the test itself.

Results for the subgroup analysis, using the higher HbA1c inclusion criterion of 8%, did not change our original conclusions. Likelihood ratio tests of the main effect of treatment had a p-value of 0.924, and both interactions with treatment-by-time and treatment-by-time squared did not reach statistical significance at p<0.05. No significant change in HbA1c by treatment assignment was observed even after the HbA1c inclusion value was raised.

Comment
One further limitation of the study might be that the results may not be completely generalizable. The patients who agreed to participate in the study might be different than the general diabetes population. It is possible that only more motivated/compliant patients agreed to participate in the study (so it possible that even the controls might be different than general population controls). Furthermore, only 50% of the participants that were eligible (when screened by phone), decided to participate in the study, even with the monetary incentive.

Response
The following has been added to the Discussion section, p.16, “Finally, findings may not be completely generalizable to adults with uncontrolled T2DM as only 49% of eligible individuals screened by phone decided to participate in the study. Of those, only 41% were randomized. Participants enrolled in our study may represent individuals who are more motivated or compliant compared to individuals with T2DM in the general population.”

Comment
The discussion section might benefit from hypothesis generation. It should try to address why the particular results might have been observed (i.e. no statistical difference). Interventions are costly and more time intensive, both for the patients and the health system, compared to usual care. Why use them? Why not just good routine care when based on your results, it seems to have the same effect (compared to the intervention).

Response
We have addressed the issue that good routine care can also lead to better glycemic control in the Conclusions section.

REVIEWER 2 (ANDRE PASCAL A KENGNE)

Comment
The study is generally well conducted and the resulting manuscript well written. Beside the challenge of conducting such a study to the standard of clinical trials (implementation of blinding procedures in particular), this particular study suffers from a selective high drop-out of participants assigned to one of the interventions (PDA), which in addition to potentially affecting the study result is a major outcome on which the authors should elaborate further and integrate in their conclusions both in the main text and the abstract. That, such a high attrition has been reported by other investigators, likely reflects the importance of accounting for the consumers’ choice in this sort of interventions. The authors may want to elaborate on such a point.
Furthermore how was the effectiveness of the training offered to participants assessed? Or the authors just assumed that after completing a training of certain duration, participants will be apt to implement self-care efficiently. What proportion of participants had used a PDA (or a similar device) before the study, and how could this impact on the learning and subsequent use of the device?

Response
Participants assigned to PDAs (PDA and CDSMP+PDA arm) were provided individual PDA instruction by a project coordinator and a supplementary reference; however, training effectiveness was not assessed. Although proficiency of PDA use was not evaluated, individuals were provided additional guidance upon request. A majority of PDA and CDSMP+PDA participants (82.2%) had no prior experience using PDAs, which may have contributed to the resistance we observed in PDA usage (Vuong et al., 2012). However, almost 90% reported prior computer use, and over 70% reported e-mail and Internet usage (Vuong et al., 2012). As such, study participants were not considered technologically inexperienced. High attrition among those using PDAs may have been due to the PDA itself, having minimal mainstream presence and thus, lower adoption rates. An additional concern is regarding PDA instruction. Since PDA overviews were provided in one session, basic use of the device may not have been achieved by study participants. PDA data was also only downloaded after participants exited the study. If data had been extracted periodically, then there would have been an opportunity to discuss concerns regarding usage of either the device or the Diabetes Pilot program. These study design factors may have contributed to low PDA use and attrition. Though PDA adoption was low, the potential benefit of electronic diabetes should not be negated. Resistance toward PDAs may have been lower had PDA training been simplified, such as having multiple sessions designed for basic and advanced users. Utilizing more familiar platforms, such as smartphones, for self-management programs may improve adoptability.

Some of these comments have already been incorporated into the revised manuscript. For example, we have included the following sentence in the Methods section: “Although proficiency with PDA use was not evaluated and individuals were provided additional guidance upon request, training effectiveness was not assessed.” We also included the following in the Discussion section: “However, it may be more beneficial to shift our focus from diabetes self-management software designed for PDAs to more mainstream devices such as smartphones and tablets. These devices have already been accepted by the general public and integrating diabetes self-management programs on these platforms would yield a more seamless transition into an individual’s daily routine.”

REVIEWER 3 (LINCOLN A SARJEANT)

MAJOR COMPULSORY REVISIONS:
Comment
The introduction notes that diabetes is more common in ethnic minorities compared to non-minorities but does not make the case for the hypothesis that "reductions in HbA1c will be more marked in minority persons with type 2 diabetes."

Response
We hypothesized that while racial/ethnic minorities may still have reduced access to healthcare their ownership rates of new technologies, such as mobile devices, may be at par with their non-minority counterparts or even higher and may therefore benefit more from a technologically-
assisted intervention such as use of a PDA. Appropriate revisions have been made in the revised manuscript.

Comment
A planned subgroup analysis was done to determine the impact of race/ethnicity on the results but no explanation given as to why 50% minority was selected. Details of the sample size calculation for the subgroup analysis should be included.

Response
The choice of 50% minority was arbitrarily made to enroll as many minorities as possible. The subgroup analysis was designed as exploratory and therefore was not factored into the sample size calculations.

Comment
Participants and their clinicians were not blind to the study groups. If participants in different arms of the study were managed in the same clinics it is possible that the behaviour of participants and clinicians could be affected by contact with the protocols in the different arms. More details are needed to help readers judge whether this could have affected the standard of usual care in the control group.

Response
We agree that due to the open label nature of the study, it was possible to have some contamination effect. This has been included as a limitation in the revised manuscript (p.15).

Comment
Additional clinical details about the participants would be helpful in comparing the results to other studies. It would be useful to know the average duration of diabetes and what proportion were controlled with insulin.

Response
Average duration of diabetes at orientation was 3.11 years (±2.44). However, it is important to note that this is likely an underestimation since we were limited to hospital records within the Scott & White Healthcare System. The earliest date a physician charted the diagnosis within Scott & White records served as the initial occurrence, but this first occurrence does not always mean that it was the very first time the patient was diagnosed with T2DM. Some patients were seen elsewhere prior to being seen at Scott & White, which would mean they were diagnosed years prior. With regard to insulin analog usage, 36.4% of study participants were on this medication according to hospital records.

Comment
Tables 2 and 3 would be more accessible if clinical data were presented showing the baseline and change in HbA1c and other variables in each study group. Similar data by ethnic subgroup would also be useful.

Response
This comment has been addressed previously.

Comment
The conclusion needs to emphasise the null finding that the interventions were not significantly better than usual care in achieving glycaemic control.

Response
We have edited the first sentence in the Conclusion, p.16, to: “In conclusion, we found that although behavioral and technological interventions can result in some modest improvements in glycemic control, these interventions did not fare significantly better than usual care in achieving glycemic control. Further research is needed to understand how these interventions can be most effective in clinical practice.”

MINOR ESSENTIAL REVISIONS:
Comment
Page 4, last paragraph - sentence should read "... serves large racially/ethnically diverse populations."
Response
The sentence has been corrected.